

We claim:

1. A compound which is a crystalline Form III of anhydrous moxifloxacin monohydrochloride.
2. The compound of claim 1 having an X-ray diffraction pattern, expressed in terms of 2θ angles and obtained with a diffractometer equipped with a copper K X-radiation source, wherein said X-ray powder diffraction pattern includes five or more peaks selected from the group consisting of peaks with 2θ angles of 5.6 ± 0.09 , 7.1 ± 0.09 , 8.4 ± 0.09 , 8.8 ± 0.09 , 10.0 ± 0.09 , 10.4 ± 0.09 , 10.4 ± 0.09 , 11.4 ± 0.09 , 12.2 ± 0.09 , 13.1 ± 0.09 , 13.9 ± 0.09 , 14.4 ± 0.09 , 14.7 ± 0.09 , 16.6 ± 0.09 , 16.9 ± 0.09 , 17.2 ± 0.09 , 17.7 ± 0.09 , 18.5 ± 0.09 , 19.1 ± 0.09 , 19.2 ± 0.09 , 19.8 ± 0.09 , 20.1 ± 0.09 , 20.3 ± 0.09 , 21.1 ± 0.09 , 21.5 ± 0.09 , 22.1 ± 0.09 , 22.6 ± 0.09 , 22.9 ± 0.09 , 23.5 ± 0.09 , 24.0 ± 0.09 , 24.6 ± 0.09 , 24.9 ± 0.09 , 25.8 ± 0.09 , 26.2 ± 0.09 , 26.6 ± 0.09 , 26.9 ± 0.09 , 27.2 ± 0.09 , 28.7 ± 0.09 , 29.1 ± 0.09 , 29.7 ± 0.09 , 30.1 ± 0.09 , 31.4 ± 0.09 , 32.1 ± 0.09 , 37.3 ± 0.09 , 39.0 ± 0.09 , 40.8 ± 0.09 , 41.5 ± 0.09 , 42.2 ± 0.09 , and 43.1 ± 0.09 degrees.
3. The compound of claim 2, wherein said X-ray diffraction pattern includes peaks with 2θ angles of about 5.6, 7.1, 8.4, 8.8, 10.0, 10.4, 10.4, 11.4, 12.2, 13.1, 13.9, 14.4, 14.7, 16.6, 16.9, 17.2, 17.7, 18.5, 19.1, 19.2, 19.8, 20.1, 20.3, 21.1, 21.5, 22.1, 22.6, 22.9, 23.5, 24.0, 24.6, 24.9, 25.8, 26.2, 26.6, 26.9, 27.2, 28.7, 29.1, 29.7, 30.1, 31.4, 32.1, 37.3, 39.0, 40.8, 41.5, 42.2, and 43.1 degrees.
4. The compound of claim 1 having an X-ray diffraction pattern, expressed in terms of 2θ angles and obtained with a diffractometer equipped with a copper K X-radiation source, wherein said X-ray powder diffraction pattern includes two or more peaks selected from the group consisting of peaks with 2θ angles of 7.1 ± 0.09 , 8.8 ± 0.09 , 13.1 ± 0.09 , 13.9 ± 0.09 , 16.6 ± 0.09 , 17.7 ± 0.09 , and 22.1 ± 0.09 .
5. The compound of claim 1 having substantially the same X-ray diffraction pattern as shown in Figure 1.
6. The compound of claim 1 having a ^{13}C solid state NMR spectrum comprising a peak at about 107 ppm.
7. The compound of claim 1 having substantially the same ^{13}C solid-state NMR spectrum as shown in Figure 2.

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8. The compound of claim 1 having an infrared absorption spectrum comprising absorption bands at about 1159 cm^{-1} and 2706 cm^{-1} .

9. The compound of claim 1 having substantially the same infrared spectrum as shown in Figure 3.

10. The compound of claim 1 having a differential scanning calorimetry thermogram, which exhibits an endotherm peak at about $246\text{ }^{\circ}\text{C}$.

11. The compound of claim 1 having substantially the same differential scanning calorimetry thermogram as shown in Figure 5.

12. The compound of claim 1 having substantially the same analytical characterization data as shown in Figures 1, 2, 3, 4, and 5.

13. A composition comprising moxifloxacin monohydrochloride as a solid, wherein at least 80% by weight of said solid moxifloxacin monohydrochloride is a crystalline form III of anhydrous moxifloxacin monohydrochloride having an X-ray diffraction pattern, expressed in terms of 2θ angles and obtained with a diffractometer equipped with a copper K X-radiation source, wherein said X-ray powder diffraction pattern includes five or more peaks selected from the group consisting of peaks with 2θ angles of 5.6 ± 0.09 , 7.1 ± 0.09 , 8.4 ± 0.09 , 8.8 ± 0.09 , 10.0 ± 0.09 , 10.4 ± 0.09 , 10.4 ± 0.09 , 11.4 ± 0.09 , 12.2 ± 0.09 , 13.1 ± 0.09 , 13.9 ± 0.09 , 14.4 ± 0.09 , 14.7 ± 0.09 , 16.6 ± 0.09 , 16.9 ± 0.09 , 17.2 ± 0.09 , 17.7 ± 0.09 , 18.5 ± 0.09 , 19.1 ± 0.09 , 19.2 ± 0.09 , 19.8 ± 0.09 , 20.1 ± 0.09 , 20.3 ± 0.09 , 21.1 ± 0.09 , 21.5 ± 0.09 , 22.1 ± 0.09 , 22.6 ± 0.09 , 22.9 ± 0.09 , 23.5 ± 0.09 , 24.0 ± 0.09 , 24.6 ± 0.09 , 24.9 ± 0.09 , 25.8 ± 0.09 , 26.2 ± 0.09 , 26.6 ± 0.09 , 26.9 ± 0.09 , 27.2 ± 0.09 , 28.7 ± 0.09 , 29.1 ± 0.09 , 29.7 ± 0.09 , 30.1 ± 0.09 , 31.4 ± 0.09 , 32.1 ± 0.09 , 37.3 ± 0.09 , 39.0 ± 0.09 , 40.8 ± 0.09 , 41.5 ± 0.09 , 42.2 ± 0.09 , and 43.1 ± 0.09 degrees.

14. A composition comprising moxifloxacin monohydrochloride as a solid, wherein at least 80% by weight of said solid moxifloxacin monohydrochloride is a crystalline Form III of anhydrous moxifloxacin monohydrochloride having an X-ray diffraction pattern, expressed in terms of 2θ angles and obtained with a diffractometer equipped with a copper K X-radiation source, wherein said X-ray diffraction pattern includes two or more peaks selected from the group consisting of peaks with 2θ

angles of 7.1 ± 0.09 , 8.8 ± 0.09 , 13.1 ± 0.09 , 13.9 ± 0.09 , 16.6 ± 0.09 , 17.7 ± 0.09 , and 22.1 ± 0.09 .

15. The composition of claim 14, wherein at least 90% by weight of said solid moxifloxacin monohydrate is in said crystalline Form III.

16. The composition of claim 14, wherein at least 95% by weight of said solid moxifloxacin monohydrate is in said crystalline Form III.

17. The composition of claim 14, wherein at least 99% by weight of said solid moxifloxacin monohydrate is in said crystalline Form III.

18. A pharmaceutical composition, which comprises a pharmaceutically effective amount of a crystalline Form III of anhydrous moxifloxacin monohydrochloride and one or more pharmaceutically acceptable carriers or diluents.

19. The pharmaceutical composition of claim 18, wherein said crystalline form III of anhydrous moxifloxacin monohydrochloride has an X-ray diffraction pattern expressed in terms of 2 theta angles and obtained with a copper K X-radiation source, wherein said X-ray powder diffraction pattern includes five or more peaks selected from the group consisting of peaks with 2 theta angles of 5.6 ± 0.09 , 7.1 ± 0.09 , 8.4 ± 0.09 , 8.8 ± 0.09 , 10.0 ± 0.09 , 10.4 ± 0.09 , 10.4 ± 0.09 , 11.4 ± 0.09 , 12.2 ± 0.09 , 13.1 ± 0.09 , 13.9 ± 0.09 , 14.4 ± 0.09 , 14.7 ± 0.09 , 16.6 ± 0.09 , 16.9 ± 0.09 , 17.2 ± 0.09 , 17.7 ± 0.09 , 18.5 ± 0.09 , 19.1 ± 0.09 , 19.2 ± 0.09 , 19.8 ± 0.09 , 20.1 ± 0.09 , 20.3 ± 0.09 , 21.1 ± 0.09 , 21.5 ± 0.09 , 22.1 ± 0.09 , 22.6 ± 0.09 , 22.9 ± 0.09 , 23.5 ± 0.09 , 24.0 ± 0.09 , 24.6 ± 0.09 , 24.9 ± 0.09 , 25.8 ± 0.09 , 26.2 ± 0.09 , 26.6 ± 0.09 , 26.9 ± 0.09 , 27.2 ± 0.09 , 28.7 ± 0.09 , 29.1 ± 0.09 , 29.7 ± 0.09 , 30.1 ± 0.09 , 31.4 ± 0.09 , 32.1 ± 0.09 , 37.3 ± 0.09 , 39.0 ± 0.09 , 40.8 ± 0.09 , 41.5 ± 0.09 , 42.2 ± 0.09 , and 43.1 ± 0.09 degrees.

20. The pharmaceutical composition of claim 18, wherein said crystalline Form III of anhydrous moxifloxacin monohydrochloride has an X-ray diffraction pattern expressed in terms of 2 theta angles and obtained with a copper K X-radiation source, wherein said X-ray powder diffraction pattern includes five or more peaks selected from the group consisting of peaks with 2 theta angles of 7.1 ± 0.09 , 8.8 ± 0.09 , 13.1 ± 0.09 , 13.9 ± 0.09 , 16.6 ± 0.09 , 17.7 ± 0.09 , and 22.1 ± 0.09 .

21. The pharmaceutical composition of claim 18, which is a solid dosage form for an oral administration.

22. The pharmaceutical composition of claim 18, wherein said solid dosage form is a tablet.

23. The pharmaceutical composition of claim 18, which is in dosage unit form containing from about 0.5 to about 800 mg of moxifloxacin monohydrochloride.

24. A process for preparation of a crystalline Form III of moxifloxacin monohydrochloride, said process comprising:

a) refluxing azeotropically a starting moxifloxacin monohydrochloride in a solvent selected from the group consisting of lower branched esters, chained acid esters, aliphatic ketones and aliphatic hydrocarbon solvents;

b) cooling the refluxed solvent while stirring the mixture until a solid separates; and

c) isolating said separated solid thereby obtaining said crystalline Form III of anhydrous moxifloxacin monohydrochloride.

25. The process of claim 24, wherein said solvent is selected from the group consisting of tertiary butyl acetate, cyclohexane, toluene, methylisobutylketone, and mixtures thereof.

26. A process for preparation of a crystalline Form III of moxifloxacin monohydrochloride, said process comprising:

a) dissolving moxifloxacin hydrochloride in a lower alkyl alcohol to obtain a solution;

b) adding to the solution an anti solvent, in which moxifloxacin hydrochloride is poorly soluble;

c) cooling the mixed solvents until a solid separates; and

d) isolating said solids thereby obtaining said crystalline Form III of moxifloxacin monohydrochloride.

27. The process of claim 26, wherein said lower alkyl alcohol is selected from the group consisting of methanol, ethanol, t-butyl alcohol, isopropyl alcohol and mixtures thereof.

28. The process of claim 26, wherein said lower alkyl alcohol is methanol.

29. The process of claim 26, wherein said anti solvent is acetonitrile.

30. The moxifloxacin monohydrochloride produced in accordance with the process of claim 24.

31. The moxifloxacin monohydrochloride produced in accordance with the process of claim 26.

32. A method of treating infections caused by susceptible strains of streptococcus pneumoniae, haemophilus influenzae, moraxella catarrhalis, haemophilus parainfluenzae, klebsiella pneumoniae, staphylococcus aureus, mycoplasma pneumoniae, Chlamydia pneumoniae and streptococcus pyogenes, which comprises administering a mammal in need thereof an effective amount of the compound of claim 1.

33. The method of claim 28, wherein said mammal is a human.